

Remarks

Claims 1, 2 4-6, 8, and 11-13 were pending in the subject application. By this Amendment, claims 1 and 4 have been amended, claims 6, 8, and 11-13 have been cancelled, and claims 17-19 have been added. The undersigned avers that no new matter is introduced by this Amendment. Support for the claim amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1, 2, 4, 5, and 17-19 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Applicants and Applicants' representative wish to thank Examiner Couch for the courtesy of the telephonic interview conducted with the undersigned on November 2, 2011, regarding the rejection under 35 USC §103(a) and potential claim amendments. The remarks and amendments set forth herein are consistent with the substance of the interview and are believed to address the outstanding issues as discussed during the interview.

By this Amendment, claims 1 and 4 have been amended, and claims 6, 8, and 11-13 have been cancelled. As suggested at page 4 of the Office Action, claim 4 has been rewritten as an independent claim. In addition, as proposed at page 4 of the Office Action and discussed during the telephonic interview, claims 1 and 4 have been amended to recite "verifying the presence of the dedifferentiated cells". Support for the amendments to claims 1 and 4, and for claims 17-19, can be found, for example, at page 5, lines 20-28, Figures 2-5; and Example 1 at page 8, lines 9-29, of the specification.

Claims 1, 2 and 4-6 remain rejected under 35 USC §103(a) as obvious over Limb *et al.* (*Investig Ophthal & Visual Sci*, 2002, 43:864-869) in view of Kelley *et al.* (*Ophthalmol Vis Sci*, 1995, 36:1280-1289). Applicants respectfully traverse.

Applicants respectfully assert that the claimed invention is not obvious over the cited references. However, in order to expedite prosecution of the subject invention to completion, Applicants have amended claims 1 and 4 to recite "verifying the presence of the dedifferentiated cells", as discussed during the telephonic interview. Applicants respectfully submit that it would not have been obvious at the time the invention was made to obtain the adult human Müller cells, culture

them to induce dedifferentiation into a progenitor phenotype, and verify the presence of the dedifferentiated cells as recited in claims 1 and 4 as amended.

The methods of claims 1 and 4 use cells obtained from the adult human retina, which express markers of mature Müller cells. In contrast, the cells disclosed by Kelley *et al* are isolated from fetal retina, and therefore do not express markers of mature Müller cells. As such, the cells used in the method of the invention are distinct from those disclosed in the Kelley *et al.* publication.

Kelley *et al.* refer to fetal human retinal progenitors; at no point do they identify Müller glia with mature markers as the source of neurons. The authors of the Kelly *et al.* publication characterize the cell types derived from their cultures as immunoreactive for neuron-specific enolase, (indicating that they are neurons), which they believed were either retinal ganglion cells or amacrine cells (see page 1282, second column, first complete paragraph). Kelley *et al.* describe proliferating cells as “flattened cells, which were probably progenitor cells or Müller cells”; however, they did not attempt to specifically characterize Müller glia with stem cell characteristics in their cultures. Furthermore, the Kelley *et al.* publication does not demonstrate that the cells they isolated were immortal, which is a characteristic of stem cells. Although the Kelley *et al.* publication demonstrates that growth factors can stimulate the proliferation of “foetal retinal progenitors”, it does not demonstrate that adult human retina harbor a population of Müller glia that exhibit mature Müller glial markers and stem cell characteristics, as required by the present claims.

The Limb *et al.* publication is co-authored by the present inventors and is an article describing the first characterization of a spontaneously immortalized Müller cell line. When this article was published, it was not known that the cells of the cell line were stem cells; this was established subsequently, following further studies. Because the nature of the cells of the invention is not disclosed in either of the cited references, it was not possible for one of ordinary skill in the art to arrive at the present claims based upon their teachings with any degree of predictability.

A rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398; 82 USPQ2d 1385 (2007). Obviousness

does not require absolute predictability; however, at least some degree of predictability is required. MPEP §2143.02. Applicants respectfully submit there would have been no reasonable expectation of success in combining the teachings of the Kelley *et al.* publication and the Limb *et al.* publication in such a way as to obtain the adult human Müller cells, culture them to induce dedifferentiation into a progenitor phenotype, and verify the presence of the dedifferentiated cells as recited in claims 1 and 4 as amended. Whether an art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986); MPEP §2141.02. Obviousness cannot be predicated on what is not known at the time an invention is made. As such, the claimed invention is not obvious in view of the cited references.

Accordingly, reconsideration and withdrawal of the rejection under 35 USC §103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicant(s) believe(s) that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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